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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/344,226	06/25/1999	RONALD H. CHIARELLO	2574.008US0	8804

7590 09/17/2002
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EXAMINER

SOLOLA, TAOFIQ A

ART UNIT	PAPER NUMBER
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1626

DATE MAILED: 09/17/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.
09/344,226

Applicant(s)
Chiarello et al.

Examiner
Taofiq A. Solola

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1626



-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on Aug 20, 2002
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1, 5-8, and 10-20 is/are pending in the application.
- 4a) Of the above, claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1, 5-8, and 10-20 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☐ All b) ☐ Some* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
*See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).
a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☒ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892) 4) ☐ Interview Summary (PTO-413) Paper No(s). _____
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948) 5) ☐ Notice of Informal Patent Application (PTO-152)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____ 6) ☐ Other:

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Claims 1, 5-8, 10-20 are pending in this application.

Claims 2-4, 9, are canceled.

Request for Continued Examination

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.117(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 8/20/02 has been entered.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1, 5-8, are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1, 5-8 are written in functional language and therefore, broader than the enabling disclosure. For example, the claim 1 recites "conjugating the fluorophore with a biomolecule" line 12, page 3, "determinable wavelength" on the last line; and claim 5 recites "attached to a

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solid support” line 1. The claims must recite how one of ordinary skill in the art would perform the conjugation or attachment. The claims must recite the reagents, the reaction times, pH, equipment, and reaction conditions involved in the process. A claim must stand alone to define the inventions, and incorporation into the claims by express reference to the specification or an external source is not permitted. Ex parte Fressola, 27 USPQ 2d 1608, BdPatApp & Inter. (1993). Applicant may not claim all processes of making conjugates of the instant compounds, known and yet to be developed. Applicant must claim only the process that embodies applicant’s invention.

Under US patent practice a process claim must recite at least one positive step. See the MPEP. The positive step must set forth the “how to” not “what.” The instantly claimed process does not recite a single positive step.

Applicants’ arguments filed 8/20/02 have been fully considered but they are not persuasive. Applicants argue that the invention should be interpreted according to the specification. “To that we all agree.” The specification discloses only one example of protein conjugation on page 27-28. The specification failed to state that the process of the example is applicable for conjugating amino acid[s], nucleotide[s], oligonucleotide[s], nucleic acid[s], cell surface membrane[s], and viral coat[s]. Therefore, if this application¹⁵ is allowed, in accordance with applicant’s contention, which I agree with, the protection is limited to the specific process of making ~~only~~ protein conjugates. Claim 1 should be amended accordingly. Also, the specification failed to state how the wavelength is determined but on page 8, disclosed excitation

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wavelength of 500-700 nm and fluorescent wavelength of 520-750 nm. Therefore, if allowed applicant's protection would be limited to these wavelentghts, provided of course, the claims recite all the relevant positive steps. Applicant also contends that there are many variety of processes of making protein conjugation. This is not persuasive because this admission is contrary to the scope of claims 1, 5-8, as set forth above.

Even then, a mere reference to another application, publication or patent is not an incorporation of anything therein into the application containing such reference for the purpose of satisfying the requirement of 35 USC 112. *In re de Seversky*, 474 F.2d 671, 177 USPQ 144 (CCPA 1973). Particular attention should be directed to specific portions of the referenced document where the subject matter being incorporated may be found. MPEP 608.01(p).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 10-20 are rejected under 35 U.S.C. 103(a) as being unpatentable over Mayer et al., US 4,647,675, in view of Earnest et al., US 4,900,686, alone and/or King US 5,846,737.

Applicants claim conjugated rhodamine dyes of generic formula 1, having several substituents. For example, R1 to R14 are each H; R2-R9 are each alkyl; Ra is alkyl, cycloalkyl

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or aryl and Z is a linker and the conjugated substance. Also, R1-R2, R5-R6, and R9 to R14 are each halogen.

Determination of the scope and content of the prior art (MPEP §2141.01)

Mayer et al., teach rhodamine dyes having formula 1, with several substituents. For example, R, R1 to R3 are each H; R4 and R5 are each alkyl, cycloalkyl; one of R4 and R5 is H or aryl; X and Y are each H or chlorine. See the abstract, specific species in columns 1-7, and claims 1-5.

Ascertainment of the difference between the prior art and the claims (MPEP §2141.02)

The difference between the instant invention and that of Mayer et al., is that in the instant invention the compounds are being claimed as conjugate while Mayer et al., do not teach the conjugates.

Finding of prima facie obviousness---rational and motivation (MPEP §2142.2413)

Earnest et al., teach rhodamine dyes are commonly used as conjugates in biological diagnostic assays, and that the most commonly used dyes are fluorescent dyes (column 1, lines 1-40). King teaches rhodamine dyes, and their method of use as conjugate of peptides, proteins nucleotides, etc. (column 1, lines 1-4). King also, teaches the conjugation of rhodamine dyes to bacteria, virus, yeast, and to immobilized solid or semi-solid support, such as polymer, membrane, polymeric particle, (microsphere), etc. See column 10, lines 10-18. Therefore, the instant invention is prima facie obvious from the teachings of Mayer et al., Earnest et al., and King. One of ordinary skill in the art would have known to conjugate the rhodamine dyes of

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Mayer et al., at the time the instant invention was made. The motivation for making the conjugates is from the teachings of , Earnest et al., and King that rhodamine dyes are useful for making conjugates.

Applicants' arguments filed 8/20/02 have been fully considered but they are not persuasive. In response to applicant's argument that the prior art of Mayer et al., is nonanalogous art, and that the prior arts of Ernest et al., and King teach different conjugation processes, it has been held that a prior art reference must either be in the field of applicant's endeavor or, if not, then be reasonably pertinent to the particular problem with which the applicant was concerned, in order to be relied upon as a basis for rejection of the claimed invention. See *In re Oetiker*, 977 F.2d 1443, 24 USPQ2d 1443 (Fed. Cir. 1992). In this case, Mayer et al., teach the same rhodamine dyes as claimed herein, and the prior arts of Earnest et al., and King teach that rhodamine dyes are well known in the art for making protein conjugates. The totality of applicant's contention is directed toward anticipatory rejection while the rejection is obviousness type. Also, the prior arts are used to reject the conjugates not the process of making them.

The Examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988) and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir.

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1992). In this case, it is well known in the art that rhodamine dyes are used in making protein conjugates. For example, see the prior arts of Earnest et al., and King above.

This is an RCE of applicant's earlier Application No. 09/344,226. All claims are drawn to the same invention claimed in the earlier application and were finally rejected on the grounds and art of record in this Office action. Accordingly, **THIS ACTION IS MADE FINAL** even though it is a first action in this case. See MPEP § 706.07(b). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no, however, event will the statutory period for reply expire later than **SIX MONTHS** from the mailing date of this final action.

Telephone Inquiry

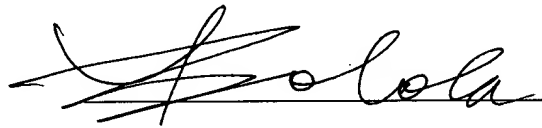
Any inquiry concerning this communication or earlier communications from the examiner should be directed to Dr. Taofiq A. Solola whose telephone number is (703) 308-4690. The

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Examiner is on flexible work schedule and the best days to get him are Mondays, Wednesdays and Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mr. Joseph McKane, can be reached on (703) 308-4537. The fax phone number for this Group is (703) 308-4556.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-1235.

A handwritten signature in black ink, appearing to read 'Taofiq A. Solola', written over a horizontal line.

Taofiq A. Solola, Ph.D.

Primary Examiner

Group 1626

September 16, 2002
